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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SHEIKH, HUMERA N	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 10/31/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/631,143	PEYMAN, GHOLAM	
	Examiner	Art Unit	
	Humera N. Sheikh	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 October 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,10-15,17,20,22,25,27,30 and 33-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,10-15,17,20,22,25,27,30 and 33-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Receipt of the Amendment after Non-Final Office Action and Applicant's Arguments/Remarks, both filed 10/05/05 are acknowledged.

The non-statutory double patenting rejection of claims 1-40 over claims 1-3 and 6-13 of copending Application No. 11/105,756 in view of Wong *et al.* (US '313) has been withdrawn, in view of Applicant's persuasive remarks.

Claims 1-8, 10-15, 17, 20, 22, 25, 27, 30 and 33-40 are pending in this action. Claims 6, 11, 15, 20, 25, 27, 30 and 37 have been amended. Claims 9, 16, 18, 19, 21, 23, 24, 26, 28, 29, 31 and 32 have been cancelled. Claims 1-8, 10-15, 17, 20, 22, 25, 27, 30 and 33-40 are rejected.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-4 are rejected under 35 U.S.C. 102(e) as being anticipated by Robinson *et al.* (US Pat. No. 6,713,081 B2).

Robinson *et al.* disclose methods for treating eye diseases and methods for delivering therapeutic agents to the eye by implanting ocular matrix-type implant devices that contain and deliver therapeutic agents for prolonged periods of time in a controlled and sustained-release manner. Suitable agents disclosed include rapamycin in effective amounts (see reference column 3, line 61 – col. 4, line 8); (col. 5, lines 10-43); (col. 25, lines 50-53) and Abstract.

Eye diseases that can be treated using the sustained-release implants include age-related macular degeneration, glaucoma, diabetic retinopathy, uveitis, retinopathy of prematurity in newborns, choroidal melanoma, chorodial mestastasis, retinal capillary hemangioma and post-corneal surgery conditions (col. 24, line 64 – col. 25, line 5); (col. 9, lines 23-31); (col. 7, lines 31-37).

The matrix-type implants comprising therapeutic agents can be secured to the sclera (col. 13, lines 40-44).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 5-8, 10-15, 17, 25, 27 and 33-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Robinson *et al.* (US Pat. No. 6,713,081 B2) in view of Kulkarni (US Pat. No. 5,387,589).

Robinson *et al.*, as delineated above, teach methods for effectively treating eye diseases by using matrix-type ocular implant devices for delivering therapeutic agents to the eye for in a sustained-release manner, whereby suitable agents disclosed include rapamycin (see reference column 3, line 61 – col. 4, line 8); (col. 5, lines 10-43); (col. 25, lines 50-53) and Abstract.

Robinson *et al.* teach that apart from implant therapies, other local administration routes for the eye have included topical delivery, such as ophthalmic drops and topical ointments containing the medicament (col. 2, lines 53-56). Other local therapy routes for the eye have involved direct intravitreal injection of a treatment drug through the sclera (col. 3, lines 25-34).

Eye diseases that can be treated include age-related macular degeneration, glaucoma, diabetic retinopathy, uveitis, retinopathy of prematurity in newborns, choroidal melanoma, chorodial mestastasis, retinal capillary hemangioma and post-corneal surgery conditions, (col. 24, line 64 – col. 25, line 5); (col. 9, lines 23-31); (col. 7, lines 31-37).

The matrix-type implants comprising therapeutic agents can be secured to the sclera (col. 13, lines 40-44). The matrix implant is particularly well-suited for subconjunctival or intravitreal placement (col. 5, lines 30-33).

Therapeutic agents that can be delivered include, for example, antibiotics, antibacterial agents, anti-glaucoma agents and immune system modifying agents, singly or in combinations thereof. Specific therapeutic agents include, in addition to rapamycin, cyclosporine A, Prograf (tacrolimus) and macrolide immunosuppressants, singly or in combinations thereof (col. 9, lines 38-52); (col. 25, line 50 – col. 26, line 42). Therapeutic agents are provided in amounts of about 1 to about 50 wt % (col. 5, lines 34-38).

According to Robinson *et al.*, the matrix implant provides an effective treatment in corneal transplantation procedures to reduce rejection rates. For example, an immune system modifier agent such as cyclosporine can be delivered non-systemically to the eye, in order to reduce the rejection rates of corneal allografts (col. 7, lines 31-37); (col. 19, lines 9-14).

The matrix also comprises polymeric substances such as polyvinyl alcohol (PVA) and poly (ethylene vinyl) acetate (col. 5, lines 44-49); (col. 7, lines 13-16).

Regarding Applicant's claims 27-29, which recite a 'therapeutic composition for treating an ocular condition', the Examiner notes that the prior art explicitly teaches ocular implants comprising therapeutic agents (*i.e.*, rapamycin) for drug delivery directed to various areas of the eye and thus the prior art recognizes how one of ordinary skill in the art would formulate the composition, per se and thus meets the claim limitations of instant composition claims 27-29.

With regards to drug concentrations, Robinson *et al.* teach therapeutic agents provided in amounts of about 1 to about 50 wt % (col. 5, lines 34-38). Robinson *et al.* do not teach the instant claimed amounts of drug (up to about 200 μg or ~3 mg - ~5mg rapamycin). However, the Examiner points out that, generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating

such concentration is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). It is the position of the Examiner that Applicants have not demonstrated any unexpected or surprising results attributable to the claimed amounts. Robinson *et al.* teach and recognize ocular matrix-type implants that contain the same therapeutic agents, such as rapamycin, formulated for sustained-release and Robinson *et al.* also teach methods for treating eye diseases using sufficient, beneficial amounts of drug (~ 1 to ~ 50 wt %), and also teach that effective results are obtained using these amounts of their invention.

As mentioned prior, Robinson *et al.* suggest that apart from implant therapies, other local administration routes for the eye have included topical delivery and also direct intravitreal injection of a treatment drug (col. 2, lines 53-56); (col. 3, lines 25-34). While Robinson *et al.* do not explicitly teach that their preferred method of administration is topical administration and/or intraocular injection, this would not deter the teaching to one of ordinary skill in the art that the prior art demonstrates how one of ordinary skill would use topical administration forms and/or intraocular injections. A preferred method teaching in the art is considered in determining patentability as well as other suggested ways that may or may not be preferable.

In any event, Kulkarni (US '589) is relied upon for the teaching of a method of treating ocular inflammation by administering an effective amount of rapamycin, whereby the rapamycin may be administered by any suitable means, including oral, topical, parenteral, intraocular,

intravitreal, intravenous, transdermal, rectal, intramuscular and subcutaneous administration (see reference column 3, lines 10-17 and Abstract).

According to Kulkarni, rapamycin may be administered topically as a solution, cream or lotion by formulation with pharmaceutically acceptable vehicles containing 0.1-5% of the active compound (col. 8, lines 4-7). Daily doses of rapamycin taught are between about 0.01-50 mg/kg/day (see col. 8, lines 8-29) and (claim 5).

Therefore, it would have been deemed obvious to one of ordinary skill in the art at the time the invention was made to modify the ocular implant drug delivery system of Robinson *et al.* to include the topical and intraocular injectable administration forms of Kulkarni, because Kulkarni teaches a method of treating ocular disorders by administering rapamycin by any suitable means, that include topical routes (*i.e.*, solution, cream) and intraocular and intravitreal injection forms and teaches that effective results are obtained using these routes of administration without harmful or deleterious side effects. The expected result would be an improved method for treating ocular disorders, which allows for ease and convenience of drug delivery to the patient.

Claims 20, 22, 30 and 37-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Robinson *et al.* (US Pat. No. 6,713,081 B2) in view of Ueno (US Pat. No. 6,872,383 B2).

Robinson *et al.*, as delineated above, teach methods for treating eye diseases and methods for delivering therapeutic agents to the eye by implanting ocular matrix-type implant

devices that contain and deliver therapeutic agents for prolonged periods of time in a controlled and sustained-release manner. Suitable agents disclosed include rapamycin in effective amounts (see reference column 3, line 61 – col. 4, line 8); (col. 5, lines 10-43); (col. 25, lines 50-53) and Abstract.

Robinson *et al.* do not teach a method to treat an ocular condition using ascomycin drug.

Ueno ('383) teaches methods for treating ocular disease, particularly dry eye disease, comprising the administration of macrolide compounds, such as ascomycin and rapamycin (see reference column 3, lines 10-19); (col. 7, lines 27-65). Ueno teaches that the macrolide compound can be administered systemically or locally, such as by oral, intravenous, subcutaneous and rectal administration forms, as well as administration to the local site in the eye (inclusive of eye ointment). Ueno also teaches that it is particularly preferable to use the form for local administration to the eye (col. 8, lines 27-36). When administered systemically, the dose is about 0.0001-1000 mg, administered in a sustained release manner. When administered locally to the eye, a preparation contains the active ingredient in a proportion of 0.001-10.0 w/v % (col. 8, lines 37-48). Dosage forms include eye drops, eye ointment, powder, granule, tablet, capsule, injection, ointment and the like, with particular preference given to eye drop and eye ointment (col. 8, lines 49-57).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the rapamycin-containing drug delivery system of Robinson *et al.* to additionally include ascomycin drug, because Ueno teaches methods for treating ocular diseases, by administering macrolide compounds, such as ascomycin and rapamycin and teaches

that these compounds are preferable and effective against diseases associated with dry eye and for the improvement of subjective symptoms, particularly dry eye, and in evaluation of tears and the like. The expected result would be a highly improved method for treating ocular disorders that provides for symptomatic relief from a variety of ocular disorders and diseases through the administration of macrolide compounds.

Response to Arguments

Applicant's arguments filed 10/05/05 have been fully considered.

Firstly, Applicant argued regarding the non-statutory double patenting rejection of claims 1-40 over claims 1-3 and 6-13 of copending Application No. 11/105,756 in view of Wong *et al.* (US '313). Applicant's arguments have been found persuasive. Accordingly, the non-statutory double patenting rejection has been withdrawn.

Secondly, Applicant argued regarding the 35 U.S.C. 102(e) rejection of claims 1-4 over Robinson ('081) stating, "Robinson does not anticipate applicant's method of treatment, at least because applicant's method provides sustained release of an effective amount of rapamycin or ascomycin. Robinson's device is either a matrix implant or a reservoir implant. The matrix contains 1-50 wt% of agent. In applicant's method, a matrix contains 3-5 mg of rapamycin and/or ascomycin; this is an amount and the agent is not formulated at a percentage of the matrix."

Applicant's arguments have been fully considered but were not found persuasive. Robinson clearly discloses methods for treating eye diseases and methods for delivering

therapeutic agents to the eye by implanting ocular matrix-type implant devices, which deliver therapeutic agents for prolonged periods of time in a controlled and *sustained-release* manner. Robinson teaches administration of the same drug, rapamycin as instantly claimed and teaches administration of rapamycin in effective amounts (see reference column 3, line 61 – col. 4, line 8); (col. 5, lines 10-43); (col. 25, lines 50-53) and Abstract. With regards to the instant claims 1-4, the Examiner notes that the claims are silent as to any particular or preferred amounts. Moreover, it is deemed obvious to one of ordinary skill in the art to determine suitable or effective amounts through routine or manipulative experimentation to obtain optimal results, as these are variable parameters attainable within the art. Applicants have not demonstrated any superior results attributable to the claimed amounts (i.e., 3-5 mg). Thus, Applicant's arguments were not persuasive.

Thirdly, Applicant argued regarding the 35 U.S.C. 103(a) rejection of claims 5-19, 25-29 and 33-36 over Robinson ('081) in view of Kulkarni ('589) stating, "Applicant disagrees with the Examiner's characterization of Robinson's drug quantity; it is 1-50% wt of the composite material. Applicant's method claims recite a concentration of agent. Claims 11-14 and 25-26 are limited to specific injected administrations, not an implantable device. For claims 15-19, while Kulkarni discloses the use of rapamycin for the treatment of ocular inflammation, there is no disclosure of the use of rapamycin to enhance ocular moisture, post-surgical or otherwise. Kulkarni discloses in connection with topical administration but not ocular topical administration, a rapamycin concentration of 0.1-5% preferably 2% (col. 8, lines 4-7). There is no disclosure of a suitable concentration for anything other than topical administration. The

claims are amended; the maximum concentrations distinguish Kulkarni because it discloses a concentration range of 0.1-5%."

Applicant's arguments have been fully considered but were not found persuasive. Examiner notes Applicant's statement of the drug quantity employed by Robinson, to be 1-50% wt. of the composite material. With regards to claims 11-14 & 25-26, Robinson teaches methods for effectively treating eye diseases in a controlled and sustained release manner. Applicant's argument that in Kulkarni 'there is no disclosure of the use of rapamycin to enhance ocular moisture, post-surgical or otherwise', was not persuasive since the prior art clearly teaches use of the same drug, rapamycin, used for the same field of endeavor as the Applicant. Since the prior art employs the same drug, it is expected that the advantages and benefits imparted by the drug (*i.e.*, rapamycin) would also be the same as when employed by Applicant. With regards to the argument that 'Kulkarni does not disclose a suitable concentration for anything other than topical administration', it is the position of the Examiner that it would have been obvious to one of ordinary skill in the art to determine suitable or effective amounts through routine experimentation to obtain the best possible results, as these are variable parameters attainable within the art. Applicants have not demonstrated any superior results attributable to the claimed amounts. The prior art teaches the use of the same drug, formulated in a similar manner, used for the same field of endeavor and to treat the same problems as that desired by Applicant. Applicants have not demonstrated that the amounts of drug disclosed by the prior art are not suitable or effective amounts.

Lastly, Applicant argued regarding the 35 U.S.C. 103(a) rejections of claims 20-24, 30-32 and 37-40 over Robinson ('081) in view of Ueno ('383) stating, "Ueno discloses topical

administration at a concentration range of 0.001-10.0 w/v%. There is no disclosure of any other form of local administration nor intraocular injection or implantation."

Applicants' arguments have been fully considered but were not found persuasive. The teachings of Robinson ('081) are delineated above. Robinson do not teach the use of ascomycin drug. The Ueno ('383) reference was relied upon solely to remedy this deficiency of Robinson by teaching that it is well known in the art to incorporate drugs, such as ascomycin or rapamycin to treat ocular-based conditions and disorders. The Ueno reference was relied upon primarily for its' teaching of ascomycin and was not relied upon for its administration methods.

Given the explicit teachings of the prior art, the instant invention, when taken as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (571) 272-0604. The examiner can normally be reached on Monday through Friday from 8:00A.M. to 5:30P.M., alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page, can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

H. N. Sheikh HNS

Patent Examiner

Art Unit 1615

October 21, 2005

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